REMARKS

By this amendment, Applicants have amended claim 1 to include a sophisticated level of control for the system. More particularly, claim 1 has been amended to include that the medical data processor is adapted to process the medical data to detect *different phases of the contrast agent's biophysical behaviour* and in response to control the amount of contrast agent administered to the subject and *the mode of data acquisition*. Support for the amendments to claim 1 can be found in the specification, for example, at page 10, lines 7 to 9 where it is stated that "[t]he analysis tool was 'in time' to detect different phases of the contrast agent's biophysical behaviour (included injection profile) which in turn controlled infusion of Gd and the acquisition protocol", and at page 8, lines 28 and 29 where it is stated that "[t]he present invention allows different image acquisition modalities to be used during different times in the protocol." Support for the amendments to claim 1 can also be found in original claims 4, 7, 8 and 10. Further, claim 1 specifies that acquisition ceases when the medical data processor has all of the pharmacokinetic parameters needed. This is based on the specification at page 10, lines 2 and 3, which states that "[a]t the point where the analysis tools have all the pharmacokinetic parameters needed, acquisition is ceased."

Claims 2, 3, 5 and 9 have been amended to include that the agent is a contrast agent and claims 6 and 11-13 have been amended to include medical image data recited in claim 1. Claims 4, 7, 8 and 10 have now been canceled, without disclaimer. These amendments do not add new matter. Applicants respectfully request entry of these amendments and allowance of the pending claims.

Rejections Under 35 U.S.C. §103(a)

The Examiner rejected claims 1-9 under 35 U.S.C.§ 103(a) as being unpatentable over U.S. Pub. No. 2002/0068865 (Meaney) in view of U.S. Patent No. 6,464,662 (Raghavan). The Examiner also rejected claims 10-13 under 35 U.S.C. 103(a) as being unpatentable over Meaney in view of Raghavan and further in view of U.S. Patent No. 6,230,041 (Prince). Applicants respectfully traverse these rejections.

Applicants respectfully submit that Meaney, Raghavan and Prince alone or in combination do not make the present claims obvious as Meaney, Raghavan and Prince disclose

relatively simple and unsophisticated feedback loops, which lack the features now in amended claim 1.

Meaney discloses a system for arterial imaging in which the timing of the imaging process can be adjusted in accordance with the arrival of the contrast agent in the artery being imaged. The aim of this is to ensure that imaging occurs when the contrast is peaking, particularly with reference to a process in which several different parts of the subject are imaged in succession, but with movement of the imaging system relative to the subject between those imaging processes. Furthermore, Meaney discloses that the rate of injection of contrast agent can be altered once the imaging system has detected contrast agent entering the region of interest. Thus whereas Meaney is concerned with optimizing the imaging process for maximal contrast, the present claims aim to obtain the best data to evaluate a particular physiological behavior. This is done by modeling of the data to compare it to what is expected, and controlling the data acquisition process accordingly. For example, in the process described bridging pages 9 and 10 of the specification, there is a first mode of data acquisition using an EPI sequence to measure an initial change in intensity which can be used to characterize regions of angiogenesis in the subject. Subsequently, though, and once the processor knows that this period is over (because it "knows", *e.g.,* has modeled, the expected biophysical behavior of the contrast agent), it switches to a different mode of data acquisition, which is used to measure the plateau of contrast agent behavior. Simultaneously the infusion of contrast agent is changed. This mode is continued until all of the desired pharmacokinetic parameters have been obtained by the processor. Then the acquisition is ceased. Thus the invention is based on the realization that knowledge of the biophysical behavior of the contrast agent, e.g. in different tissue types, allows you to obtain more information about the subject (not just a better image) if you adjust the acquisition mode and administration dynamically in response to *processed* image data. This is a more sophisticated level of control than is possible in Meaney.

Meaney simply looks for maximum contrast to start its main imaging process. It has no "knowledge" of the contrast agent's biophysical behavior and it does not disclose switching the mode of data acquisition simultaneously with administration of the contrast agent. Nor does it disclose detecting different phases of the agent's biophysical behavior (still less switching acquisition mode and administration mode in response). Nor does Meaney disclose ceasing

acquisition at the point where all of the pharmacokinetic parameters have been obtained. The advantage of the claimed features is that the adjustment of the acquisition mode and administration of an agent with the biophysical behavior can improve the results obtained by reducing false positives, false negatives and artifacts, and can allow more detailed information to be obtained about the subject being imaged. Thus, starting from Meaney, which discloses obtaining an image more reliably (but basically the same image as before) by timing acquisition to correspond to maximum contrast, the problem is how to obtain wider and more detailed information on the subject from the image. The presently claimed features solve this problem by adapting the medical data processor to detect different phases of the agent's biophysical behavior and in turn adjusting the amount of agent administered *and* adjusting the mode of data acquisition. Further, the data acquisition continues until all of the desired pharmacokinetic parameters have been obtained. Meaney does not disclose these features.

Meaney also lacks the specific features regarding the real-time analysis of the behavior of the contrast agent, namely the characterization of the uptake and wash-out of contrast agent to provide pharmacokinetic parameters. Meaney also lacks the specific feature that the mode of data acquisition is controlled to provide an optimized trade off between spatial and temporal resolution in the different phases of the contrast agents biophysical behavior.

Like Meaney, none of these features are known from Raghavan or Prince. More particularly, Raghavan discloses a method of drug delivery, which is planned in advance and can be controlled by a computer. Using scan-visibility of the injected substance the computer monitors deviations from the plan and can pause the injection, or generate a new plan of infusion/injection, which it can implement autonomously. However, Raghavan lacks any suggestion that the mode of data acquisition is changed by the computer. Further the computer does not model the uptake and wash-out of contrast agent to produce pharmacokinetic parameters. Further, Raghavan does not disclose any form of trade off between spatial and temporal resolution in different phases of the contrast agent's biophysical behavior. As mentioned above, Raghavan is a relatively simple form of feedback loop. In Meaney the feedback is simply used to start the imaging process at the point of maximum contrast. In Raghavan the feedback is simply to monitor for compliance with the plan, and in the event of a deviation, to adopt a new injection plan.

With the presently claimed features, on the other hand, by processing in real time the image data obtained throughout the process it is possible to obtain the pharmacokinetic parameters and to control the image acquisition process accordingly. It is important to note the fact that the pharmacokinetic models are fitted in real-time and require that the image data is reconstructed into actual images in real-time. It is also interesting to note that the fitting of a pharmacokinetic model requires a measured input function. In the present application, this is obtained by imaging the uptake part of the curve. This is not necessary in the cited prior art of Meaney, Raghavan, and/or Prince.

Because the presently claimed features include real-time analysis of the behavior of the contrast agent in the subject to characterize the uptake and wash-out of contrast agent, it is possible in practice for it to modify the imaging protocol, for example by prolonging the acquisition. This could be done, for example, if the fitting of the pharmacokinetic model was not sufficiently accurate. The presently claimed features also enable changes of mode such as having a low spatial resolution but high temporal resolution imaging process in the uptake phase of contrast enhancement, followed by a slow, high spatial resolution process in the wash-out phase. This gives the advantage that the fast uptake characteristic of angiogenesis of a tumor can be seen in the high temporal resolution sequence, whereas in the slower wash-out phase a greater spatial resolution can be achieved to allow location of the tumor. None of these features are disclosed in Meaney, Raghavan, and/or Prince. Thus in summary the cited prior art does not disclose the idea of changing the mode of data acquisition in different phases of the contrast agent's behavior, with this behavior being detected by modeling its pharmacokinetic behavior.

Accordingly, Meaney, Raghavan, and/or Prince do not render the present claims obvious and one of ordinary skill in the art would not combine these cited references the way the Examiner combines them. Even if one of ordinary skill in the art would combine them the way the Examiner does, one still would not obtained the present claims. Applicants respectfully submit the claims cannot be considered obvious over any of the cited references alone or in combination and request that the rejections under 35 U.S.C. §103(a) be reconsidered and withdrawn.

Conclusion

Reconsideration and allowance are respectfully solicited.

Applicants hereby request a two-month extension of time under 37 CFR 1.136(a) and Request for Continued Application and authorizes the Patent Office to charge Kalow & Springut LLP's credit card. No additional fee is believed to be due with respect to filing this amendment. If any additional fees are due, or an overpayment has been made, please charge, or credit, our Deposit Account No. 11-0171 for such sum.

If the Examiner has any questions regarding the present application, the Examiner is cordially invited to contact Applicants' attorney at the telephone number provided below.

Respectfully submitted,

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